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Significance Of Thyroid Autoantibodies, Thyroid Function And ASST In Chronic Idiopathic Urticaria --- A Clinical Study

KEYWORDS: Chronic Urticaria, Thyroid autoantibodies, Autologous serum skin test.

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ABSTRACT *Background: Chronic urticaria comprises 25% among patients of urticaria. The prevalence of thyroid function alterations, and thyroid autoantibodies increasing in urticaria patients inspired us to undertake the present study. Materials and Methods: A total of 100 patients of chronic urticaria of 6 weeks duration attending to the department of dermatology during the period of 12 months were enrolled. Autologous serum skin test, Thyroid hormones,Thyroid autoantibodies were performed to all cases. Results: 3465 patients were presented with urticaria constitutes 12.1% of total number of patients attended during the period of 12 months. In this study group of 100 patients of chronic urticaria, ASST was positive in 46%, Thyroid autoantibodies was positive in 27%. Mean age of patients studied was 34.11 years. The mean duration of urticaria was 21.6 months and 13 months in TGA positive and TGA negative groups respectively. The significant female preponderance was observed (p>0.05). Abnormal thyroid function was seen in 8 patients. Conclusion: ASST,Thyroidprofile,and thyroid autoantibodies were considered to be screening tests for autoimmune urticaria. Thyroid dysfunction tests helps the patients who are likely to have more severe disease and require new modalities of treatment.*

Introduction

Urticaria was described in 1772 by Heberden as "nettle rash" appears involuntarily and seldom stays many hours in the same place[1]. Urticaria is common dermatoses observed in 15-25% of general population and 25% of urticaria is chronic(Leznoff)[2]. Chronic urticarial is characterized by recurrent, itchy, transient appearance of wheals with or without angioedema lasting for more than six weeks(Fig1).

Figure 1: Urticarial lesions on the back

Patients with urticaria have considerable distress and it causes impairment in the quality of life and make the condition frustrating for both the patient and physician[3,4,5]. Despite of extensive investigations, no cause is identified in the majority, thus remains idiopathic. The prevalence of thyroid function alterations and ever changing explanations on its pathogenesis have often induced unseen confusions and challenges in therapeutic approach of the disease[6]. It has been reported in previous studies, that the presence of antithyroid antibodies such as antithyroglobulin (TGA), antimicrosomal antibodies (TMA) and antithyroperoxidase antibodies (TPO) were significantly higher in patients with chronic urticaria (Zauli et al 2001). The present study was carried out to found the abnormalities of thyroid profile and thyroid autoantibodies, autologous serum skin test in chronic idiopathic urticaria patients attending the department of Dermatology at Govt general hospital attached to medical college from june 2012 to june 2013.

Materials And Methods

This prospective analytical study was conducted in the Department of Dermatology at Govt general hospital attached to medical college. The period of study was 12 months from june 2012 to june 2013. A total of 100 patients of chronic urticaria of more than six weeks duration, were enrolled after the washout period, for the particular medication, ranges from 21 days to 90 days for different drugs. All the patients were between the ages of nine to sixty years of age, willing for investigations and other tests, included in the study. Exclusion criteria include physical urticaria, cholinergic urticaria, Hereditary angioedema, urticaria due to medications, insect bites, food allergy, connective tissue diseases, vasculitis, neoplasms, mast cell disease, acute and chronic infections, pregnancy and lactation. A detailed clinical history includes duration of disease, frequency, distribution and duration of wheals, associated systemic symptoms (fever, joint pains, abdominal pain), angioedema, provoking factors, food and drug intolerance were noted. All the patients were subjected to physical provocation tests by using standard methods. To rule out systemic causes of urticaria, routine laboratory investigations like complete blood examination, urine examination, liver function tests, renal function tests, C_3 and

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C_4 complement levels and antinuclear antibodies were done. Autologous serum skin test was performed to all the patients(Fig 2).

Figure 2 Intradermal injection of the test serum

5ml venous blood of the patient was drawn with a sterile, disposable syringe, and it was subjected to centrifugation using centrifuge machine at the rate of 2000rpm for 10 min at room temperature. 0.05ml of the serum thus separated was injected immediately intradermally into the patients left flexor forearm.0.05ml of sterile normal saline as negative control into the right arm using 1ml BD insulin syringe. The beveled end of the needle was kept in the upward direction producing a palpable bleb on the skin. A reading of wheal was taken after 30min, patients having wheal of more than 1.5mm were considered to be ASST positive(Fig 3,4).

Figure3:Positive ASST showing wheal formation and er-

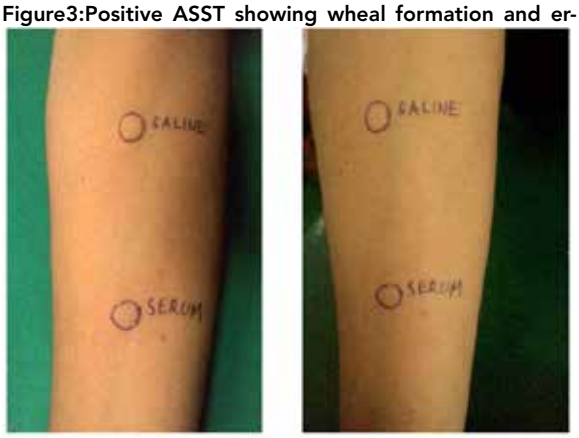

Figure4: Negative ASST

All the patients were investigated for thyroid function tests, thyroid autoantibodies vizantimicrosomal antibodies and antithyroglobulin antibodies. Demographic frequencies were expressed as mean±standard deviation or as percentage distribution. The relationship between urticaria duration, history and autoantibodies was evaluated by using t test and chi-square test, when appropriate p value of <0.05 was considered statistically significant.

Results

A total of 100 patients of chronic urticaria were enrolled in the study. A total of 28, 626 attended the outpatient department of Dermatology during the period of 12 months, 3465 patients were presented with urticaria which consti-

Table no 1. ASST positivity in chronic urticaria patients:

ASST	Number	Percentage
Positive	46	46%
Negative	54	54%
Total	100	100 %

(Table 1). Among 100 patients, 27 patients (27%) were positive for thyroid autoantibodies and 73 patients were negative (Table 2).

Table – 2 : Thyroid Autoantibodies positivity in chronic urticaria patients:

Thyroid auto antibodies	Number	Percentage
Positive	27	27%
Negative	73	73%
Total	100	100%

The mean age of the patients studied was 34.11 years (Table 3).

Table - 3 Age distribution of chronic urticaria patients:

The mean age of the patients studied was 34.11 years.

Age Distribution	Anti thyroid Auto Antibodies		Total
	Positive	Negative	
9 – 20 years	2 (7.4%)	8 (10.9%)	10 (10%)
21 – 30 years	4 (14.8%)	15 (20.54%)	19 (19%)
31 – 40 years	15 (55.5%)	34 (46.5%)	49 (49%)
41 – 50 years	5 (18.5%)	13 (17.8%)	18 (18%)
More than 50 years	1 (3%)	3 (4.1%)	4 (4%)

There is no significant difference in the age distribution between thyroid autoantibodies positive and negative patients (chi square test value 1.147 p>0.05). There is significant female preponderance was observed out of 100 cases, 72 were females, 21(77.8%) were positive for TGA and out of 28 males, 6 patients(22.2%) were positive TGA (chi

Table – 4 : Sex distribution in chronic urticaria patients:

Sex Distribution	Anti thyroid Auto Antibodies		Total
	Positive	Negative	
Male	6 (22.2%)	22 (30.1%)	28(28%)
Female	21 (77.8%)	51 (69.9%)	72 (72%)
Total	**27 (100%)**	**73 (100%)**	**100 (100%)**

Chi square test value: 0.2199 p> 0.05 (0.6391) [NS]

square test value 0.2199 p>0.05) (Table 4). The mean duration of chronic urticaria was 21.6 months and 13 months in TGA positive and TGA negative groups respectively. The

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mean absolute eosinophil count in TGA positive patients was 300.10±165.08 and it was 370.85±170.31 in TGA negative t test value 1.8593 (p>0.05). Abnormal thyroid function was seen in 8 patients, 7 of them being thyroid autoantibodies positive, 1 patient being thyroid autoantibodies negative. Of 8 patients, 7 patients had hypothyroidism and 1 patient had hyperthyroidism (Table 5).

Table – 5 : Thyroid function test in chronic urticaria patients:

TFT	Anti thyroid Auto Antibodies		Total
	Positive	Negative	
Normal	20[74.07%]	72[98.63%]	92[92%]
Hypothyroid	6[22.22%]	1[1.36%]	7[7%]
Hyperthyroid	1[3.70%]	0	1[1%]
Total	**27[100%]**	**73[100%]**	**100[100%]**

Discussion

Chronic idiopathic urticaria was a commondermatoses has been classified as autoimmune on the basis of two main findings, association with thyroid autoimmunity and anti IgE and/or anti IgE receptor antibodies[7]. There is growing evidence in some cases of CIU are associated with thyroid autoimmunity. Patients with CIU have an increased frequency of Hashimato's thyroiditis with the presence of antibodies to thyroglobulin or a microsomal derived antigen (peroxidase), even in euthyroid patients. Antibodies reactive with Fc_eRI, the high affinity IgE receptor are found in sera of 10-40% of patients with CIU[8]. In the literature, there is no data to suggest that any of the antithyroidantibodies is pathogenic in terms of CIU, and most likely these are associated parallel, autoimmune events. Screening for thyroid autoimmunity and function is advisable in all patients with CIU for the early identification of patients requiring either treatment of underlying thyroid dysfunction or followup. This inspire us to undertake the present study, 100 clinically diagnosed cases of urticaria patients attending the outpatient department of Teaching hospital, were included.

The incidence of urticaria patients attending the OPD in our study was 12.1%, which was almost similar to 10.8% in the study done by Ferrer M et al.Out of 100 patients[9] ASST was positive in 46% of patients. Earlier studies reported it was about 25-50%. A positive test was suggestive but not diagnostic of autoimmune basis of urticaria. Confirmation is done by in vitro testing for anti Fc_eRI and anti IgE antibodies. Positive ASST incidence in our study correlates with the study of Vohraet al[10], Sabroeet al[11], Asero et al[12] found ASST positive in 31% and 67% respectively. An Indian study Godse KV[13] found 26.67% ASST positive in 45 CIU patients. In a recent study by mamata G et al[14] there were 34 ASST positive out of 100 patients.Nimiet al[15], found 60% of the 163 patients to be positive for ASST positive. Zweimannet al[16] and Tonget al[17] found 30% and 50% respectively.

In the present study, positive thyroid autoantibodies were obtained in 27 patients(27%), negative in 73 patients(73%). Leznoff A et al[18], found thyroid autoimmunity in 12.1%. Cebeci F et al [19], compared the frequency of thyroid autoantibodies in 140 CIU patients with 181 age and sex matched volunteers. The frequency of thyroid autoantibodies was significantly higher in patients with CIU than that healthy controls (29.28%/5.52% p<0.001). Of 41 patients, 10 had thyroid dysfunction. There was no difference in age distribution between thyroid autoantibodies positive and negative groups in our study. The mean age was 34.11 years and age ranged from 9-56 years. Out of 100 patients, 72(72%) patients were females and 28(28%) were males. This finding concurs with female preponderance in CIU found in other studies[20,11].

The mean duration of disease was 21.6 months and 13 months in thyroid autoantibodies positive and negative groups respectively. The longer the duration of disease can be explained by the inability and difficulty in controlling autoimmune urticaria.

Absolute Eosinophil count in thyroid autoantibodies positive group was 300.10±165.08 and in negative group was 370±170.31. Of the total of 100 patients, 8 patients showed thyroid dysfunction. Of them 7 patients were thyroid autoantibodies positive and 1 patient was hyperthyroid. The above results were comparable to study done by Ceberi F et al[19], who compared the frequency of thyroid autoantibodies in 140 patients with 181 age and sex matched volunteers. The frequency of thyroid autoantibodies was significantly higher in patients with CIU than that of healthy controls (29.28% / 5.52, p<0.001). Of 41 patients,10 had thyroid dysfunction.

In the present study, we observed there is no significant differencesin the severity of the disease in CIU patients with or without thyroid dysfunction. These findings confirm to the previous study which stated that patients may still suffer from CU after three years or even more, despite absence of hypothyroidism. Furthermore, in this study, among patients of CU of more than three years duration, the frequency of antithyroid antibodies positivity increases significantly. Thus early identification of patients whose urticaria is expected to be chronic warrants an immunological work up. If TGA and TMA are present in high titers, this may support the diagnosis of chronic immunologic urticaria.

Conclusion

In one hundred patients of study group chronic urticaria was predominantly seen between 31-40 years of age. The incidence was more common in females (1:2.57). Mean duration of disease was more in thyroid autoantibodies positive group of patients. Thyroid autoantibodies were positive in 27% of patients and thyroid dysfunction was seen in 25% of thyroid autoantibodies patients. ASST was positive in 46% of patients. The mean age was not significantly different between the ASST positive and negative groups. Mean AEC count was lower in thyroid autoantibodies positive group.

Thus ASST, Thyroid profile and thyroid autoantibodies are considered to be screening tests for autoimmune urticaria. It helps in the identification of a subgroup of patients who likely to have more severe disease and require new modalities of treatment.

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